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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,725	09/04/2004	Daniel W Chan	57203(71699)	7047
21874 7590 06/04/2008 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
YAO, LEI				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/506,725

Applicant(s)

CHAN ET AL.

Examiner

LEI YAO

Art Unit

1642

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-58 is/are pending in the application.
- 4a) Of the above claim(s) 14, 15, 20, 22 and 32-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13, 16-19, 21, 23-31 and 58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Response to Arguments and Amendment

The Amendment filed on 2/18/2008 in response to the previous Non-Final Office Action (9/17/2007) is acknowledged and has been entered.

Claim 58 is added.

Claims 1-58 are pending.

Claims 14, 15, 20, 22, and 32-57 have been withdrawn for non-elected invention.

Claims 1-13, 16-19, 21, 23-31, and 58 are pending and the claims, drawn to a method of qualifying or determining a breast cancer by measuring at least one marker (elect BC3) and a method of measuring of a plurality of biomarkers comprising BC3 (elected), are under consideration.

The following office action contains NEW GROUNDS of rejection based on new considerations.

Specification

It is acknowledged that the specification is amended to delete hyperlink.

Rejections Withdrawn

The rejection of claims 32-33 and 35-36 under 35 USC § 102 as being anticipated by Murray et al., is withdrawn in view of the cancellation of the claims.

Claim Objections

Claims 1-13, 16-19, 21, 23-31, and 58 are objected to because of the following informalities: The claims recite measuring biomarker, Marker I (BC1), Marker II (BC2), Marker III (BC3)etc. The specification although teaches the molecule weight of the biomarkers, BC1 is about 4.3 kD, BC2 is about 8.2 kD, BC3 is about 8.9 kD,etc. measured by SELDI mass spectra [0137], neither specification, nor the claims provide more information such as full name, the abbreviation recognized in the art, or the structures such as sequences or SEQ ID NOs of the biomarkers.

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Since neither claims nor specification define or provide the recognized names in the art or the structures of the biomarker, BC1, BC2, or BC3, etc. in the claimed method the following rejections are based on two different interpretations of these biomarkers in the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 16-19, 21, 23-25, and 58 are rejected under 35 U.S.C. 112, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that in this rejection, the biomarkers, BC2, and BC3 in the claimed method are considered as truncated plasma complement protein, anaphylatoxin C3a, lacking the C-terminal region I (see below for the detail).

The claims are drawn to a method of qualifying breast cancer (claim 1) in a subject or determining if a subject has breast cancer (claim 58) comprising measuring at least one biomarker listed in claim 1 and 58 in a sample such as BC1, BC2, or BC3 etc. and correlating the measurement with the breast cancer status comprising the presence or absence of breast cancer.

It is noted that the specification teaches that "breast cancer status" refers to the status of the disease in the patient and that examples of types of breast cancer status include, but are not limited to, the subject's risk of cancer, the presence or absence of disease, the state of disease in a patient, and the effectiveness of treatment of disease (page 5, lines 5-9). Thus, for examination purposes the terms "qualifying breast cancer" and "breast cancer status" are interpreted to include assessing the disease state in the subject, including lymph node involvement, metastasis and tumor burden, and assessing the subject's risk of breast cancer.

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The specification teaches that mass spectrometry protein profiles of serum specimens from stages 0-1 breast cancer were compared against those of non-cancer controls to identify potential cancer biomarkers that can detect early breast cancer (Examples 1-3). The specification further teaches that the ability of these identified biomarkers to detect breast cancer was independently tested using samples from Stage II and III cancer patients and that the top scoring peaks were BC1, BC2 and BC3 (Examples 1-3). The specification further teaches that BC1 (also designated as Marker I) has a molecular weight of 4.3 kD, that BC2 (also designated as Marker II) has a molecular weight of 8.1 kD and that BC3 (also designated as Marker III) has a molecular weight of 8.9 kD (page 3). The specification further teaches that the BC3 marker identified 88% of stage 0-1 patients, 78% of stage II patients, and 92% of stage III patients and that a composite analysis using the BC1, BC2 and BC3 markers identified 93% of stage 0-1 patients, 85% of stage II patients, and 93% of stage III patients. The specification further teaches that the composite analysis using the BC1, BC2 and BC3 markers showed a high sensitivity (93%) and specificity (91%) and that the detection of the 8.9 kD protein performed the best of the individual markers with a sensitivity of 85% and a specificity of 91% (Example 6). The specification further teaches that in an analysis of ductal carcinoma in situ sample and lobular carcinoma in situ samples, the expression patterns of two of the markers (the 8.9 kD protein and the 8.1 kD protein) were consistent with previous results (Example 6). The specification contemplates, in one aspect of the invention, that the patient sample is selected from the group consisting of blood, blood plasma, serum, urine, tissue, cells, organs and vaginal fluids (page 8, lines 4-6). The specification further teaches that the sample is preferably a biological fluid sample, and that examples of a biological fluid sample blood, blood serum, plasma, nipple aspirate, urine, tears, saliva, etc. (page 32, lines 23- 25).

The teaching of the specification cannot be extrapolated to enable the scope of the claims because one of skill in the art could not predict that the broadly claimed method of qualifying breast cancer would function as claimed. In particular, the art teaches that an independent validation of the previously identified breast cancer biomarkers (BC1, BC2, and BC3) shows that BC3 was identified as being anaphylatoxin C3a lacking the C-terminal region (i.e. C3a_{desarg}) and BC2 was identified as being a C-terminal-truncated form of C3a_{desarg}, wherein C3 is a molecule of the human complement system that is

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cleaved into C3b and C3a, wherein C3a is very short lived in serum and is cleaved immediately into the more stable C3a_{desarg} (Li et al., inventor of the instant application, 2005, Clinical Chemistry 51(12):2229-2235; page 2229 and 2233, provided 9/17/2007). Li et al. also teaches that higher C3 concentrations were reported with neuroblastoma patients and that higher complement concentrations were reported in patients with lung digestive tract, and brain tumors (page 2234). Li et al. also teaches that the BC1 marker was not confirmed because previous studies (i.e. the instant specification and Li et al., 2002, Clinical Chemistry 48:1296-1304) showed a BC1 decrease in breast cancer, whereas the Li et al., 2005, teaches that an increase of BC1 was associated with cancer (page 2231). Further, in commenting on the studies of Li et al. (2005), Diamandis (2006, Clinical Chemistry 52(4):771, provided 9/17/2007) notes that there was no difference between patients with benign breast disease and invasive cancer for BC2 and that there was no difference among patients with benign breast disease, ductal carcinoma in situ, of invasive carcinomas for BC3 (page 771). Diamandis further states that C3 is a high abundance serum protein whose serum concentration is increased or decreased in a wide variety of clinical conditions and that proteolytic processing of peptides in circulation by peptidases are well known and it should not be surprising that the identified molecules represent modified or truncated forms of C3a (page 771). Diamandis concludes that the BC2 and BC3 markers are likely non-specific biomarkers of acute phase reactions and are likely of questionable clinical value (page 771).

Thus given the teaching in the art that the marker BC1 was not validated, that BC2 and BC3 were not able to distinguish between benign breast disease and cancer, that complement, C3, and C3a are levels are known to vary in variety of clinical conditions and acute phase reactions, and that proteolytic cleavage of circulatory proteins is known to be prevalent, one of skill in the art could not predict that measuring BC3 levels or BC2 levels, i.e. proteolytic products of C3 and C3a, would be useful in qualifying breast cancer as claimed because altered levels of BC3 or BC2 are likely to be found in benign breast disease or in other clinical conditions as taught by Diamandis. Thus, practice of the invention would require undue experimentation.

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Response to Applicant's argument:

The response filed 2/18/2008 has been carefully considered but is deemed not to be persuasive to overcome the rejection because Applicant merely provide the teachings in the specification (page 9-11), not address the issues discussed in the rejection, especially BC1 considered as an validated biomarker for breast cancer by applicant's own publication as well as the comment by Diamandis on no difference between the patients with benign breast disease and invasive breast diseases (see rejection above).

Applicant on page 12 further argues that

the Examiner cites a number of references to support the enablement rejection, but each of these references was published after the priority date of the instant application. Enablement is determined as of the effective filing date of the patent, In re Hogan, 559 F.2d 595, 604 (CCPA 1977).

In response, right after the citation of In re Hogan, the section of MPEP 2164.05 state:

If individuals of skill in the art state that a particular invention is not possible years after the filing date, that would be evidence that the disclosed invention was not possible at the time of filing and should be considered.

The Applicant's own publication has invalidated the biomarker BC1 for breast cancer determination and the art has indicated no difference of BC2/BC3 between the benign and cancer condition. Both references although published after filing the application give a strong support for the Office's position, that is disclosed invention was not possible at the time of filing, which should be considered. Thus, Applicant's argument has not been found persuasive and the rejection is made again.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section

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351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1, 2, 4, 5, 7, 13, 16, 17, 23, 25, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Watson et al., (US Patent No. 5855889, issued 1999).

The claims are drawn to a method of qualifying or determining a subject having breast cancer comprising: measuring at least one biomarker as such BC3 (elected) in a sample from a subject and correlating the measurement with breast cancer status, wherein further comprising managing subject treatment based on the status, and measuring the biomarker after treatment, wherein the sample is blood and measuring and quantifying the marker by immunoassay.

It is noted that specification although teaches the molecule weight (MW) of the biomarkers BC3 at about 8.9, neither the specification, nor the claims provide information including the full name, or detailed structure such as sequences of the markers in the cells comprising BC3. Thus, in this rejection by given the broadest interpretation, the biomarkers recited in the claims are interpreted as any biomarkers with same or similar molecule weight as the markers recited in the claims (also see 112 1st rejection above with different interpretation). Watson et al., disclose a method of detecting or determining breast cancer by measuring the serum levels of 93 amino acid mammaglobin having MW about 9 kD (SEQ ID NO: 2). The mammaglobin has the similar MW as the Marker III BC3. Watson et al., disclose that the mammaglobin is present in the blood sample and measured by immunoassay [0021, 0033]. Watson et al., also disclose that the marker could be used for monitoring the disease status or the recurrence of the disease after treatment, the determining preferred therapeutic regimen for the patient [0018] and for determining the stage of breast cancer (bridging col 6-7).

The method appears to meet the requirements of the instant claims regarding to the method steps and the presence of the biomarker in the blood for breast cancer patient. The prior art although does not name mammaglobin such as BC3 or BC2, the mammaglobin has the similar MW as BC3 or BC2 as described in the specification. However, regarding to the structure of BC3, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics of the product in the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to

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prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

2. Claims 1, 2, 4-8, 10, 11, 17-19, 21, 23, 24, 26-28, 30 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Mutter et al., (US Patent No. 6703204, priority to July 28, 2000).

The claims are drawn to a method of qualifying or determining a subject having breast cancer comprising: measuring one or polarity of biomarkers comprising BC3 (elected) in a sample from a subject and correlating the measurement with breast cancer status, wherein further comprising managing subject treatment based on the status, and measuring the biomarker after treatment, wherein measuring and quantifying by protein chip and SELDI mass spectra or immunoassay and wherein analyzing by classification, wherein further comprising measuring a known marker.

It is noted that specification although teaches the MW of the biomarkers, neither the specification, nor the claims provide information including the full names, the structure or function of the marker in the cells comprising elected BC3 (MW about 8.9 kD), BC2 (MW about 8.1 kD) and other markers having MW from about 4 kD to 18 kD. Thus, the claims are given the broadest interpretation as any biomarker in the samples measured by immunoassay comprising immunohistochemistry and mass spectroscopy for detecting or determining breast cancer.

Mutter et al., disclose a method of detecting or determining breast cancer or other diseases by measuring and comparing one or a polarity of biomarkers that are present or absent in the tissues (lymph node) samples from the breast cancer or other patients as well as monitoring the treatment (abstract). Mutter et al., disclose a method step of measuring the marker(s) by immunohistochemistry with antibody labeled, mass spectrum (SELDI) with ProteinChip system (col 16) and protein array (col 19, line 13+) to quantify the presence or absence of the biomarkers for the breast cancer status comprising diagnosing, monitoring treatment or progression/regression, classifying the tumors with algorithm (col 2, line 50+, col 23). Mutter et al., also disclose the method including measuring a known marker (table 1).

Since the specification and claims do not define that the structures of the biomarkers in the method and do not specifically indicate that the biomarkers are the full length of the proteins or the fragments of the proteins detected by Mass Spectrum, the proteins having the same or the similar

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molecule weights, for example, about 80 amino acids of SEQ ID NO: 64, 65, (MW is about 8 kD), etc. meet the limitation of the biomarkers, for example, BC2 or BC3, in the claims. However, regarding to the structures or the sequence of the biomarker, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the product in the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
-
1. Claims 1-3, 8-12, 26, 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al., (US Patent No. 5855889, issued 1999) or Mutter et al., (US Patent No. 6703204, priority to July 28, 2000) in view of Lauro et al (Anticancer Res. vol 19, page 3511-5, 1999, abstract) and/or Gion et al., (Clin. Chem. vol 45, page 630-637, 1999).

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The claims 1 and 26 are set forth above, wherein the method further comprise measuring a known biomarker CA15-3 or CA 27.29 and managing a treatment based on the status of the cancer.

The teachings of Watson et al., and Mutter et al., are set forth above.

Neither Watson nor Mutter et al., teach the method comprising the marker CA15-3 or CA 27.29.

Lauro et al., teach a method of detecting or monitoring breast cancer therapy by the levels of marker CA15-3 or CA 27.2. Lauro et al., also teach that the patient is subjected for anticancer treatment (abstract).

Gion et al also teach a method of measuring marker CA15-3 or CA 27.2 in the primary breast cancer (entirety of reference).

It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art." SEE *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and MPEP 2144.06.

It is *prima facie* obvious to combine the methods to qualify or determine a breast cancer and or monitor or manage the treatment or progression/prognosis of the breast cancer with additional marker CA15-3 or CA 27.2 with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to add an additional known marker(s) in the method in order to increase the efficacy or accuracy of the method for monitoring or determining the breast cancer status because both Lauro et al., and Gion et al., suggest that CA15-3 or CA 27.2 are valuable marker for the breast cancer diagnosis or monitoring. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings to arrive the claimed invention because both CA15-3 and CA 27.2 are known biomarkers for breast cancer being taught by Lauro and Gion et al., and Watson et al., and/or Mutter et al., have shown the method of measuring one or a plurality of biomarkers in the serum or tissues from breast cancer patients. Therefore, the references in combination teach every limitation of the claims and the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

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Since the specification and claims do not define that the structures of the biomarkers in the method and does not specifically indicate that the biomarkers are the full length of the proteins or a fragment of the protein detected by a Mass Spectrum or immunoassay, the protein having the same or the similar molecule weight, for example, about 80 amino acids of SEQ ID NO: 64, 65, etc (MW is about 8 kDa) meet the limitation of the biomarker, for example, BC2 or BC3, in the claims. However, regarding to the structures or the sequence of the biomarker, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the product in the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

2. Claims 26 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mutter et al., (US Patent No. 6703204, priority to July 28, 2000) in view of Watson et al., (US Patent No. 5855889, issued 1999).

Claim 26 is set forth above, wherein the sample is from blood or serum or plasma (claim 31).

The teaching of Mutter et al on a method of measuring a polarity of biomarker comprising a marker having molecule weight in the tumor sample is set forth above.

Mutter et al do not teach a method of measuring the biomarkers in the blood related sample. However, the markers disclosed in the reference of Mutter et al., are soluble protein, which would or could be present in the blood of an individual (table 1)

Watson et al., teach a method of measuring a marker in the blood sample by an immunoassay (see 102(b) rejection above).

It is *prima facie* obvious to combine the two methods to measuring a plurality of marker in the blood sample with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to measure the markers in the blood in order to determine and use the

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markers presented in the blood to avoid invasive assay for the cancer diagnosis because some of the markers taught in the Mutter et al., are known to as a secreted protein, which could be found the blood (for example, IGF1, table 1). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to do so because Mutter et al., have shown the biomarker and Watson et al have already shown the method. Therefore, the references in combination teach every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Since the specification does not define that the structures of the biomarkers and does not specifically indicate that the biomarkers are the full length of the proteins or a fragment of the protein detected by immunoassay, the protein having the same or the similar molecule weight as BC2 or BC2 described in the specification would meet the limitation of the claims (for example, about 80 amino acids of SEQ ID NO: 64, 65 etc). However, regarding to the structures or the sequence of the biomarker, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the product in the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643